COMPREHENSIVE DENTISTRY:

HEPATITIS UPDATE

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COMPREHENSIVE DENTISTRY:

HEPATITIS UPDATE

AT LEAST SEVEN TYPES OF VIRAL HEPATITIS ARE RECOGNIZED

- TYPE A (HAV)
- TYPE B (HBV)
- TYPE C (HCV)
- TYPE DELTA (HDV)
- TYPE E (HEV)
- TYPE G (HGV and GBV-C)

ANNUAL INFECTION and DEATH RATE in U.S.

- 5 MILLION AMERICANS ARE CHRONICALLY INFECTED WITH THREE FORMS OF HEPATITIS
- MORE THAN 15,000 DIE EACH YEAR FROM COMPLICATIONS OF HEPATITIS
- INFECTION RATE AT LOWEST POINT IN 26 YEARS

SOURCE: RN December 1997

ANNUAL INFECTION and DEATH RATE in U.S.

	INFECTS	DEATH RATE
HAV	7,500	Rare
HBV	200,000	4,000 - 5,000
HCV	150,000	8,000 - 10,000
HDV	13,000	
HDE	? - DIFFICULT TO DIAGNOSE	

 SOURCE: RN December 1997

REGARDLESS OF THE SPECIFIC AGENT INVOLVED, A VARIABLE CLINICAL PICTURE MAY OCCUR

- ASYMPTOMATIC ANICTERIC INFECTION
  - WITHOUT JAUNDICE
- MILD SYMPTOMATIC ANICTERIC INFECTION
- CLASSIC ICTERIC INFECTION
  - WITH JAUNDICE
- FULMINANT HEPATITIS

DIFFERENTIAL DIAGNOSIS FOR ACUTE VIRAL HEPATITIS

- **VIRAL ILLNESSES** (MONONUCLEOSIS)
- **SPIROCHETAL DISEASES** (SECONDARY SYPHILIS)
- **RICKETTSIAL DISEASES** (Q FEVER)
- **DRUG INDUCED** -TOXIC RXN (ETOH, APAP, SEX HORMONES) HYPERSENSITIVITY RXN - HALOTHANE, CHLORPROMAZINE, METHYLDOPA)

THREE PHASES OF "CLASSIC" HEPATITIS

- **PRODROMAL PHASE**
  - Flu-like symptoms
- **ICTERIC PHASE**
  - Jaundice
- **CONVALESCENT PHASE**
  - Recovery

PRODROMAL PHASE

- MALAISE, HEADACHE, FEVER, MYALGIA, ARTHRALGIA, EASY FATIGABILITY
- UPPER RESPIRATORY SYMPTOMS
- ANOREXIA
- AVERSION TO CIGARETTES

ICTERIC PHASE

- UPPER RIGHT QUADRANT PAIN
- HEPATOMEGALY
- SPLENOMEGALY
- JAUNDICE
- INCREASED UROBILINOGEN - RESULTS IN DARK URINE

CONVALESCENT PHASE

- INCREASED SENSE OF WELL BEING
- RETURN OF APPETITE
- DISAPPEARANCE OF JAUNDICE, ABDOMINAL PAIN, AND TENDERNESS

LAB TESTS

AST AND ALT RESULTS

- ELEVATION INDICATES HEPATIC CELL DAMAGE / NECROSIS
- 10 TO 100 FOLD INCREASE CAN BE EXPECTED
- IF ALT IS DISPROPORTIONATELY LOW COMPARED TO AST, ALCOHOLIC HEPATITIS IS MORE LIKELY THAN VIRAL HEPATITIS

LAB TESTS

SERUM ALKALINE PHOSPHATASE

- EXHIBITS LITTLE OR NO CHANGE IN VIRAL HEPATITIS
- A LARGE INCREASE IS SEEN IN IMPAIRED BILE EXCRETION SUCH AS CHOLESTATIC HEPATITIS

LAB TESTS

SERUM BILIRUBIN

- **RISE AFTER OCCURRENCE OF LIVER DAMAGE**
- **LEVELS MUST APPROACH 3mg/100ml TO MANIFEST AS JAUNDICE**
  - **WHY MOST CASES ARE ANICTERIC**
- **JAUNDICE OFTEN FIRST MANIFESTS IN SCLERA**
- **OFTEN COMPLAIN OF SEVERE ITCHING** (PRURITUS)

LAB TESTS

BLOOD TESTS

- WBC COUNT MAY BE SLIGHTLY ELEVATED
- RELATIVE LYMPHOCYTOSIS
- ATYPICAL CELLS MAY BE PRESENT
  - LIKE INFECTIOUS MONONUCLEOSIS
- HIGHER THE PROTHROMBIN TIME (PT), THE

  MORE SEVERE THE HEPATIC DAMAGE

HEPATITIS TYPE A (HAV)

- AGENT A 27nm SINGLE-STRANDED RNA VIRUS (NO ENVELOPE)
- GENUS *HEPATOVIRUS* WITHIN THE FAMILY *PICORNAVIRIDAE*
- SPREAD MAINLY BY ORAL-FECAL ROUTE
- SEXUAL TRANSMISSION MAY OCCUR

HAV

- **CONDITIONS WHICH PROMOTE SPREAD OF HAV :**
  - **CROWDING, i.e. SCHOOLS, MILITARY, INSTITUTIONS, DAY CARE CENTERS**
  - **POOR SANITATION RESULTING IN WATER CONTAMINATION**

HAV

- IN INFECTED INDIVIDUALS, VIRUS IS PRESENT IN BLOOD AND STOOLS 14-21 DAYS BEFORE ONSET OF JAUNDICE
- VIRUS IN STOOLS DISAPPEARS BEFORE PEAK LIVER ENZYME ELEVATION OR JAUNDICE ONSET

HAV

- ACTUAL LIVER DAMAGE PROBABLY A IMMUNOLOGICAL RXN, NOT SIMPLE VIRAL REPLICATION
- 30-40% U.S. ADULTS HAVE BEEN EXPOSED TO HAV
- INCUBATION PERIOD 15-50 DAYS
- PRODROME, IF PRESENT, IS SUDDEN AND MAY MIMIC INFLUENZA OR GASTROENTERITIS

HAV

- USUALLY DISEASE OF YOUNG, OFTEN ASYMPTOMATIC
- ADULT PATIENT WILL COMMONLY MANIFEST JAUNDICE
- ILLNESS USUALLY SELF-LIMITING RECOVERY IS COMPLETE
- NO EVIDENCE OF CHRONIC FORM OR CARRIER STATE OF HAV

HAV

- **TWO-DOSE VACCINE**
  - **6 MONTHS APART**
  - **AVAILABLE SINCE 1994**
- **HEALTH CARE PROVIDERS -*RECOMMENDED***
- **INTERNATIONAL TRAVELERS AT RISK FOR INFECTION - ARE ENCOURAGED TO HAVE COMPLETE SERIES BEFORE TRAVEL**

HEPATITIS B (HBV)

- HB VIRUS STRUCTURALLY MORE COMPLEX THAN HAV
- CLASSIFIED IN *HEPADNAVIRIDAE* FAMILY
- CAN CAUSE A WIDE VARIETY OF ACUTE / CHRONIC AND EXTRAHEPATIC DISEASES, AND A CHRONIC CARRIER STATE

HBV

- DANE PARTICLE IS THE COMPLETE VIRION
- IT'S A SPHERICAL PARTICLE WITH DIAMETER OF 42 nm
  - AN INNER CORE (27 nm IN DIAMETER)
  - OUTER SHELL, WHICH IS A 14 nm LIPID ENVELOPE

HBV INNER CORE

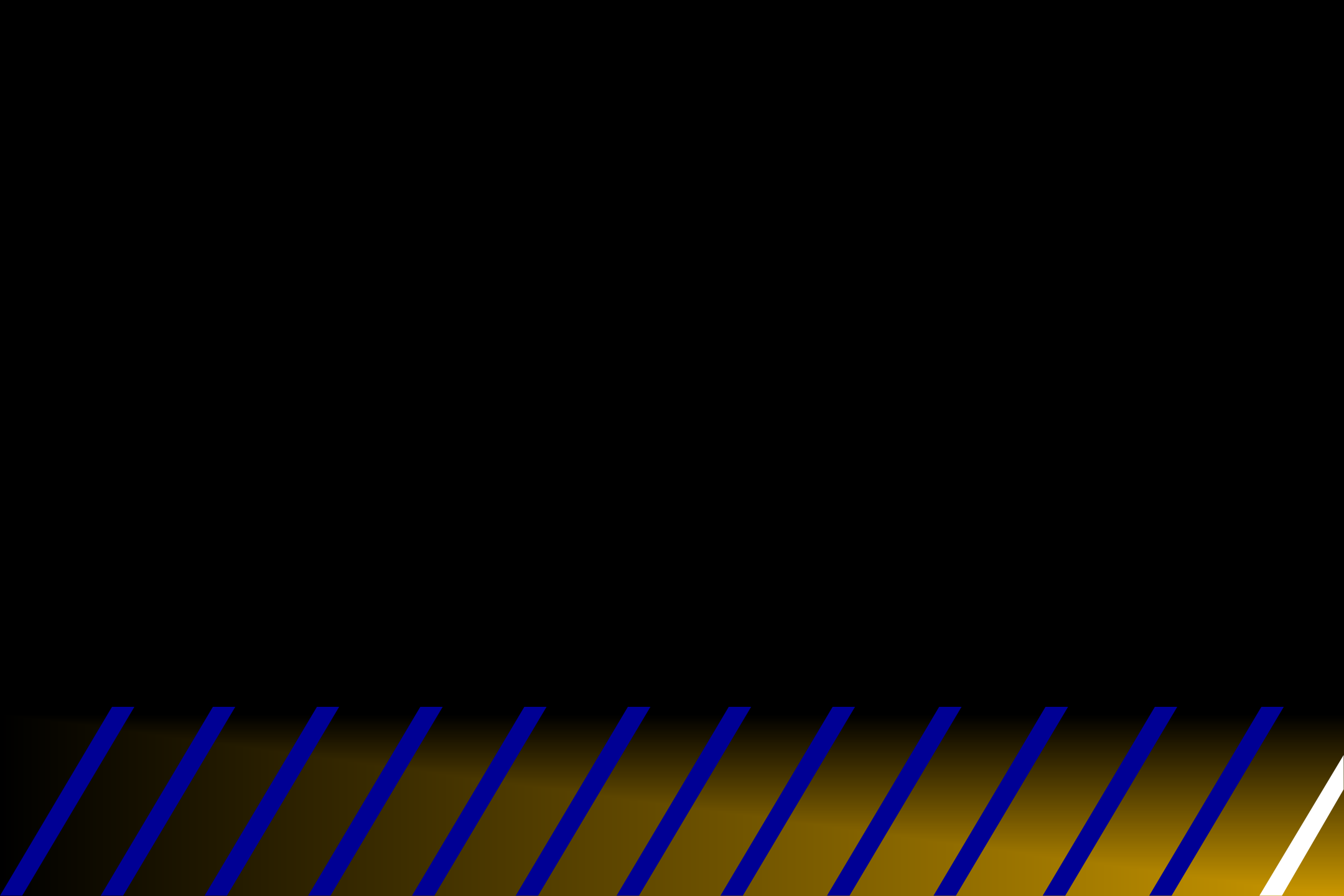
- HBV CORE ANTIGEN (HBcAg)
- HBV “e” ANTIGEN (HBeAg)
  - CORRELATES WITH HBV REPLICATION AND HIGH INFECTIVITY
- PARTIALLY SINGLE STRANDED CIRCULAR DNA
- DNA POLYMERASE

HBV OUTER SHELL

- CONTAINS HBV SURFACE ANTIGEN (HBsAg)
- HBsAg IS A MARKER FOR INTACT DANE PARTICLE
- FOUND ON SURFACE OF VIRUS AND 22 nm SPHERICAL / TUBULAR FORMS
- AT LEAST FOUR ANTIGENIC SUBTYPES

HBV

- HBV IS SYNTHESIZED ONLY IN THE HEPATOCYTE
  - HBcAg MADE IN NUCLEUS
  - HBsAg MADE IN CYTOPLASM
- 40 - 180 DAY INCUBATION PERIOD
- MANY CASES ARE SUBCLINICAL AND MOST ARE ANICTERIC



HBV SPREAD MAINLY BY PARENTERAL ROUTE

- DIRECT PERCUTANEOUS INOCULATION OF INFECTED SERUM OR PLASMA
- INDIRECTLY THROUGH CUTS OR ABRASIONS
- ABSORPTION THROUGH MUCOSAL SURFACES
- ABSORPTION OF OTHER INFECTIOUS SECRETIONS (SALIVA OR SEMEN DURING SEX)

HBV SPREAD MAINLY BY PARENTERAL ROUTE

- POSSIBLE TRANSFER VIA INANIMATE ENVIRONMENTAL SURFACES
- VERTICAL TRANSMISSION SOON AFTER CHILDBIRTH (TRANSPLACENTAL TRANSFER RARE)
- CLOSE, INTIMATE CONTACT WITH AN INFECTED PERSON

WHO IS AT GREATEST RISK FOR HBV INFECTION?

- IV DRUG ABUSERS
- BLOOD PRODUCT RECIPIENTS
  - ACCOUNTS FOR 5-10% POSTRANSFUSION HEPATITIS
- HEMODIALYSIS PATIENTS
- PEOPLE FROM SOUTHEAST ASIAN COUNTRIES (70-80%)

WHO IS AT GREATEST RISK FOR HBV INFECTION?

- LAB PERSONNEL WORKING WITH BLOOD PRODUCTS
- SEXUALLY ACTIVE HOMOSEXUALS
- PERSONS WITH MULTIPLE AND FREQUENT SEX CONTACTS
- MEDICAL/DENTAL PERSONNEL

HBV

- 300,000 NEW CASES IN U.S. PER YEAR
- LIFETIME RISK FOR AVERAGE PERSON IS 5%
- SEXUAL PROMISCUITY > RISK
- LIFETIME RISK FOR DENTIST IS 13-28%

HBV

- LIKE HAV, ACTUAL LIVER DAMAGE PROBABLY IMMUNOLOGICAL RXN
  - IMMUNE RXN TO HBcAg IN LIVER
  - IMMUNE RXN TO HBeAg, DANE PARTICLE, DNA POLYMERASE, AND HBcAg IN THE SERUM

HBV

- EXTRAHEPATIC MANIFESTATIONS
  - SERUM SICKNESS-LIKE SYNDROME
  - MEMBRANOUS GLOMERULONEPHRITIS
- RELATED TO CIRCULATING IMMUNE COMPLEXES (HBsAg, ANTI-HBs)

HBV

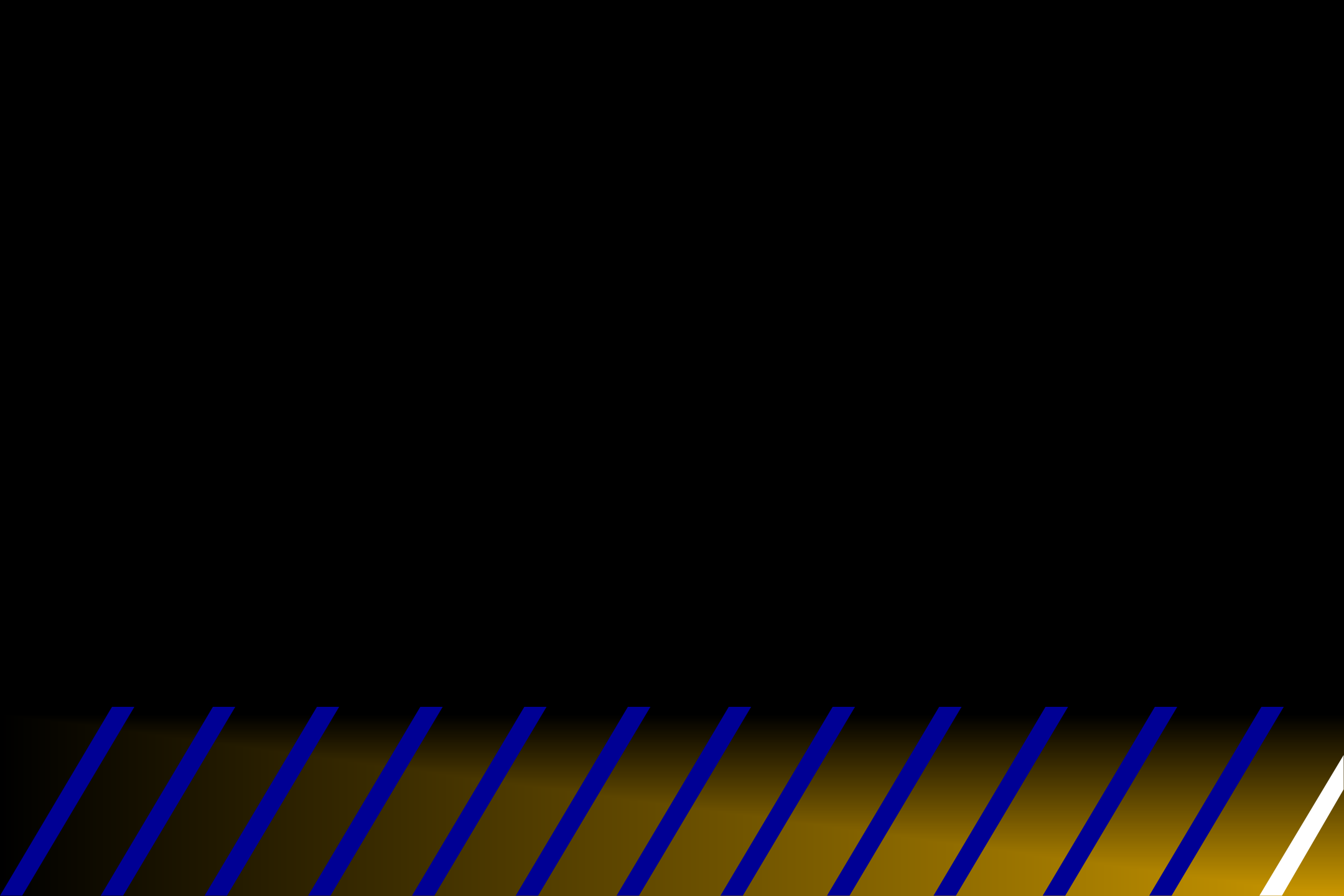
- "CORE ANTIBODY WINDOW" IS THE PERIOD DURING WHICH THERE IS NO EVIDENCE OF HBsAg OR ANTI-HBs
- ONLY MARKER AT THIS TIME IS ANTI-HBc TITER
- PATIENT IS INFECTIOUS DURING THIS TIME

OTHER CHARACTERISTICS OF HBV INFECTION

- DISEASE OF YOUNG ADULTS
- PARENTERALLY ACQUIRED INFECTION MORE LIKELY TO PRODUCE CLINICAL DISEASE
- CLINICAL ONSET SIMILAR TO HAV
  - MORE INSIDIOUS AND PROTRACTED
  - WITHOUT HEADACHE OR FEVER

OTHER CHARACTERISTICS OF HBV INFECTION

- INFECTION IS USUALLY SELF LIMITING, COMPLETE RESOLUTION IN 6 MONTHS
- HOWEVER, WHEN INFECTED
  - 5% ADULTS CHRONIC CARRIERS
  - 20% CHILDREN CHRONIC CARRIERS
  - 80-90% NEONATES AND INFANTS BECOME CHRONIC CARRIERS



HEPATITIS C (HCV)

- FORMERLY KNOWN AS PARENTAL FORM NON-A NON-B HEPATITIS
- 30 TO 60 nm RNA VIRUS
- FAMILY *FLAVIVIRIDAE*
- SPREAD MAINLY BY PARENTAL ROUTE

HCV

- ACCOUNTS FOR 90-95% OF POST TRANSFUSION HEPATITIS
- RISK OF SEXUAL TRANSMISSION LOWER THAN FOR HBV
- RISK THROUGH CASUAL CONTACT LOW

HCV

- VERTICAL TRANSMISSION POSSIBLE
  - RISK INCREASED IF MOTHER IS POSITIVE FOR HCV RNA
  - RISK INCREASED IF MOTHER IS HIV POSITIVE
- OVERALL PREVALENCE ESTIMATED AT 1.4%

WHO IS AT GREATEST RISK FOR HCV INFECTION?

- IV DRUG ABUSERS
- BLOOD PRODUCT RECIPIENTS (ANTI-HCV SCREENING HAS GREATLY REDUCED RISK)
- HEMODIALYSIS PATIENTS
- LAB PERSONNEL WORKING WITH BLOOD PRODUCTS

WHO IS AT GREATEST RISK FOR HCV INFECTION?

- SEXUALLY ACTIVE HOMOSEXUALS
- PERSONS WITH MULTIPLE AND FREQUENT SEXUAL CONTACTS
- MEDICAL/DENTAL PERSONNEL (3-10% VIA NEEDLESTICK FROM INFECTED PATIENT)

OTHER CHARACTERISTICS OF HCV INFECTION

- APPEARS TO BE CYTOPATHIC TO LIVER CELLS
- 30-180 DAY INCUBATION PERIOD
- UP TO 80% ARE ANICTERIC AND ASYMPTOMATIC
  - ANTI-HCV IS NOT PROTECTIVE AND SLOW TO DEVELOP
  - UP TO 90% = CHRONIC CARRIERS

OTHER CHARACTERISTICS OF HCV INFECTION

- SEROLOGIC DEMONSTRATION OF ANTI-HCV DOES NOT OCCUR FOR WEEKS TO MONTHS
- PROVIDES A PROLONGED UNDETECTED WINDOW DURING WHICH THE PATIENT CONTINUES TO BE INFECTIOUS

OTHER CHARACTERISTICS OF HCV INFECTION

- CHRONIC HCV PATIENTS USUALLY HAVE FEW CLINICAL SIGNS OF LIVER DISEASE
- HOWEVER, PERSISTENT VIRAL INFECTION CAN PREDISPOSE TO:
  - LATER HEPATIC FAILURE
  - HEPATOCELLULAR CARCINOMA

OTHER CHARACTERISTICS OF HCV INFECTION

- PRESENCE OF ANTI-HCV DOES NOT DISTINGUISH BETWEEN ACUTE OR CHRONIC HCV
- POSITIVE IMMUNOGLOBULIN TEST CANNOT DISCRIMINATE BETWEEN A PERSON WHO HAS RECOVERED FROM HCV FROM ONE WHO IS A CHRONIC CARRIER

HCV NOT EASILY TRANSMITTED IN HEALTH CARE SETTING

POTENTIAL TRANSMISSION RISK TO HEALTH CARE WORKERS

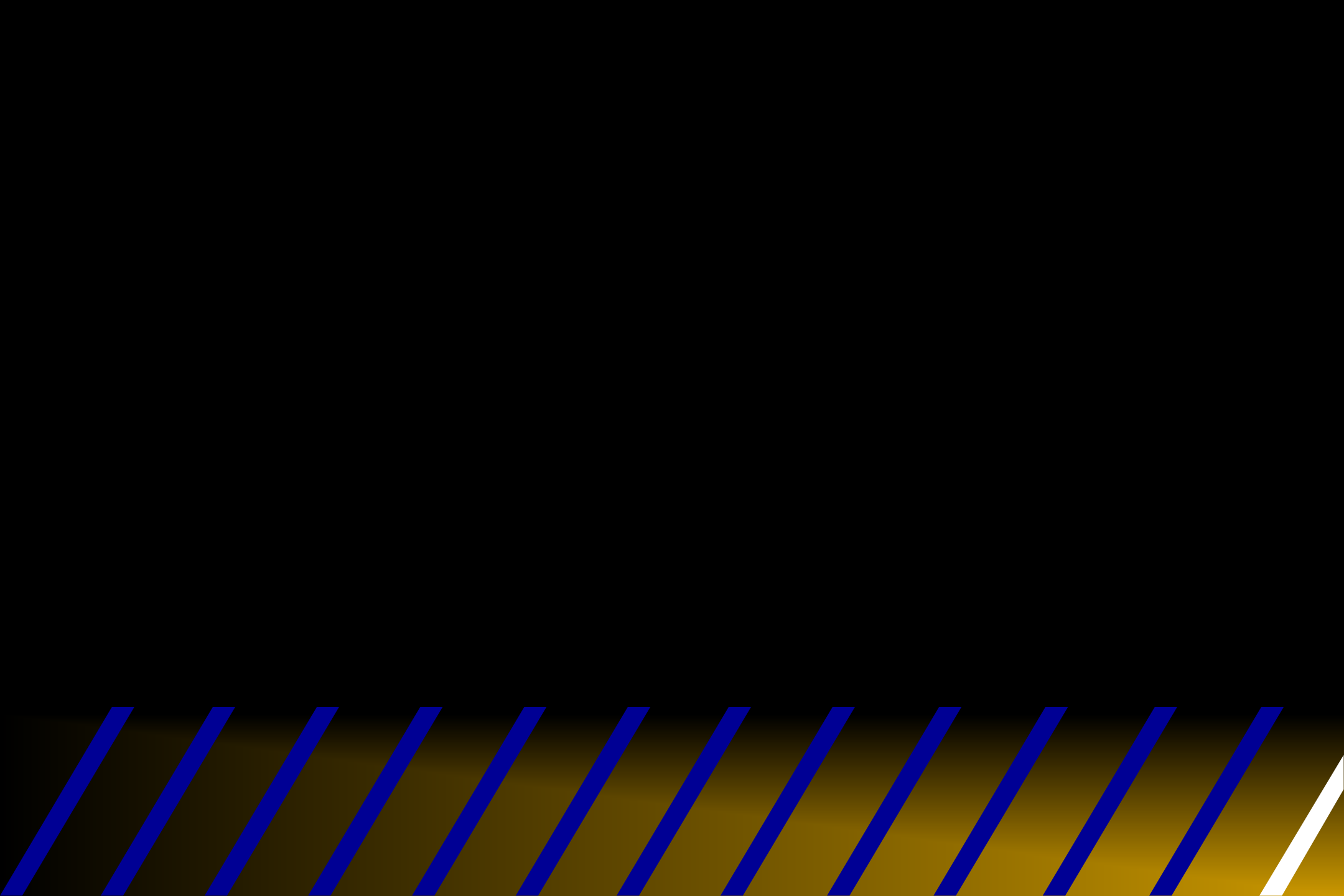
PATHOGEN	CONC/ml SERUM/PLASMA	TRANSMISSION RATE (%) POST NEEDLESTICK INJURY
HBV	1000 - 100,000,000	6.0 - 30.0
HCV	10 - 1,000,000	2.7 - 6.0
HIV	10 - 1000	0.31

BP LANPHEAR: EPIDEMIOL REV 16:437, 1994.

GOOD NEWS ON HEPATITIS C

TAKING THEIR CUE FROM AIDS ESEARCH, DOCTORS HAVE DISCOVERED THAT A COCTAIL OF DRUGS MAY BE MORE EFFECTIVE THAN A SINGLE MEDICATION AGAINST HEPATITIS C. UNTIL NOW INTERFERON - INJECTED THREE TIMES A WEEK - WAS THE ONLY TREATMENT. BUT STUDIES SHOW THAT ADDING THE ANTIVIRAL PILL RIBAVIRIN CAN MORE THAN DOUBLE THE ODDS OF ERADICATING THE LIVER DISEASE. AND FOR THOSE WHO SUFFER A RELAPSE, THE COMBO INCREASES THE CHANCES FOR A SUCCESSFUL TREATMENT FIVEFOLD.

 SOURCE: **TIME** November 30, 1998



HEPATITIS D (HDV)

- HIGHLY PATHOGENIC FORM OF VIRAL HEPATITIS (Delta)
- LOW MOLECULAR WEIGHT RNA GENOME ENCLOSED IN PARTICLE COATED WITH HBsAg
- 35-37 nm DIAMETER

HDV

- IT IS A DEFECTIVE VIRUS WHICH NEEDS HBV TO REPLICATE
- SEROLOGIC TEST FOR ANTI-HDAg EXISTS BY AVAILABILITY LIMITED
- WORLD WIDE DISTRIBUTION
  - GREATER IN MEDITERRANEAN BASIN
  - LOW IN SOUTHEAST ASIA

HDV

- TRANSMISSION SIMILAR TO HBV
- PROBABLY CYTOPATHIC TO HEPATIC CELLS
- TWO PATTERNS OF INFECTION DESCRIBED (Coinfection & Superinfection)
- BOTH HAVE INCREASED MORBIDITY COMPARED TO HBV

HDV INFECTION PATTERNS

- **COINFECTION**
  - ACUTE SIMULTANEOUS INFECTION WITH HBV AND HDV
  - OFTEN RESULTS IN FULMINANT INFECTION (70% CIRRHOSIS)
  - SURVIVORS RARELY DEVELOP CHRONIC INFECTION (< 5%)

HDV INFECTION PATTERNS

- **SUPERINFECTION**
  - **RESULTS IN HDV SUPERINFECTION IN AN HBsAg CARRIER (CHRONIC HBV)**
  - **CAN OCCUR ANYTIME DURING CHRONIC DISEASE**
  - **USUALLY RESULTS IN RAPIDLY PROGRESSIVE SUBACUTE OR CHRONIC HEPATITIS**

HEPATITIS E (HEV)

- FORMERLY KNOWN AS ENTERIC FORM OF NON-A NON-B HEPATITIS
- UNCLASSIFIED VIRUS
- ENDEMIC TO SouthEast AND CENTRAL ASIA, FORMER SOVIET UNION, AFRICA AND MEXICO (None in US)
- NO SEROLOGIC TEST AVAILABLE

HEV

- INFECTION FOLLOWS PATTERN SIMILAR TO HAV INFECTION
- 6 - 8 WEEK INCUBATION PERIOD
- FECAL-ORAL / H20 TRANSMISSION
- MILD CLINICAL COURSE (MORTALITY < 1%)
- FATALITY RATE APPROACHES 20% FOR WOMEN IN 3RD TRIMESTER OF PREGNANCY

HGV AND GVB-C

- SHARE 95% AMINO ACID IDENTITY
- THUS REPRESENT DIFFERENT ISOLATES OF THE SAME HUMAN VIRUS

 SOURCE: DIGESTION 1997; 57

HGV

- “HEPATITIS C-LIKE VIRUS”
- CLASSIFIED IN THE *FLAVIVIRIDAE* FAMILY → SAME AS HCV
- GENETIC ORGANIZATION
  - → SIMILAR TO HCV
  - → GENONE CONSISTS OF SINGLE-STRANDED RNA MOLECULE OF POSITIVE POLARITY

 SOURCE: DIGESTION 1997; 57

HGV - EPIDEMIOLOGY

- TRANSMISSABLE BY BLOOD AND BLOOD PRODUCTS
- PRESENT IN ASYMPTOMATIC BLOOD DONORS WITH NORMAL ALT LEVELS
- FOUND IN:

GENERAL POPULATION	1-2 %
HEMOPHILIA PATIENTS	18 %
IV DRUG USERS	33 %
Patients with chronic Hepatitis B	10 %
Patients with chronic Hepatitis C	20%

 SOURCE: DIGESTION 1997; 57

HGV - CLINICAL SIGNIFICANCE

- RECENT DATA SUGGESTS:
  - HGV INFECTION DOES NOT CAUSE ACUTE HEPATITIS
  - HGV MAY ESTABLISH CHRONIC INFECTIONS
  - FREQUENTLY OCCURS WITH HBC AND HCV INFECTIONS
  - MAY NOTQUALIFY AS A TRUE HEPATITIS VIRUS

CHRONIC HEPATITIS

- CHRONIC FORMS OF HBV, HBV / HDV, AND HCV INFECTIONS ARE RECOGNIZED
- FOR HEALTH CARE PROVIDER, CHRONIC HBV CAUSES GREATEST CONCERN AND HAS BEEN MOST STUDIED

CHRONIC HBV

- A CARRIER IS DEFINED BY SEROLOGIC PERSISTENCE OF HBsAg FOR 6 MONTHS
- CARRIERS DEVELOP LITTLE ANTI-HBs AND THUS REMAIN HBsAg- POSITIVE
- HAVE SUSTAINED LEVELS OF ANTI-HBc AND HBeAg

CHRONIC HBV

- LIKELIHOOD OF DEVELOPING THE CARRIER STATE VARIES INVERSELY WITH AGE AT WHICH PERSON IS INFECTED (> IF YOUNGER)
  - DURING PERINATAL PERIOD, HBV TRANSMITTED FROM HBeAg- POSITIVE MOTHERS RESULTS IN HBV INFECTION IN UP TO 90% OF THE INFANTS
  - 6-10% ACUTELY INFECTED ADULTS BECOME CARRIERS

CHRONIC HBV

- CARRIERS DEVELOPING AN ASYMPTOMATIC SUBCLINICAL INFECTION MORE LIKELY TO BE HBsAg POSITIVE
- THEY ARE MORE INFECTIOUS AND CONTAGIOUS = GREATER RISK OF TRANSMITTING THE DISEASE
- 1 MILLION HBV CARRIERS IN U.S.!

CHRONIC HBV

- MAY BE GENETIC BASIS FOR DEVELOPING THE CARRIER STATE (AUTOSOMAL RECESSIVE)
  - GREATER SOUTHEAST ASIANS, 3RD WORLD
  - PROGRESSION TO HBV CARRIER GREATER AFTER ANICTERIC THAN ICTERIC INFECTION
  - GREATER IN MEN THAN WOMEN

CHRONIC HBV

- CARRIERS MAY BE HEALTHY OR EXHIBIT CHRONIC DISEASE
- "HEALTHY" CARRIER ONLY HAS ↑ HBsAg AND IS MONITORED
- CHRONIC DISEASE CARRIER HAS ↑ HBsAg, HBeAg, HBV DNA, ↑ SERUM LIVER ENZYME LEVELS, ↑ RISK OF CIRRHOSIS/HEPATOMA
  - TX WITH INTERFERON ALPHA-2b

CHRONIC HCV

- 2-3 MILLION CARRIER OF HCV IN U.S.
- DIAGNOSIS BASED ON PRESENCE OF ANTI-HCV
- PRESENCE OF ↑ LIVER ENZYMES AND HCV RNA INDICATES MORE ACTIVE DISEASE
- NATURAL PROGRESSION OF CHRONIC HCV QUITE VARIABLE

CHRONIC HCV

- RISK OF CIRRHOSIS 20-30%
- RISK OF HEPATOMA UNDER 20%
- MANY PATIENTS EXPERIENCE AN INDOLENT COURSE
- MILD CASES ARE MONITORED
- MORE ACTIVE DISEASE TREATED WITH INTERFERON ALPHA-2b

FULMINANT VIRAL HEPATITIS

- RARE AND OCCURS IN LESS THAN 1% OF ICTERIC HEPATITIS INFECTIONS
- SEVERE, PROGRESSIVE MANIFESTATION OF VIRAL HEPATITIS
- CAUSES EXTENSIVE LIVER CELL NECROSIS

FULMINANT VIRAL HEPATITIS

- LIVER MAY SUDDENLY BECOME SMALLER
- MARKED ↑ IN PROTHROMBIN TIME (PT), THAT DOES NOT IMPROVE WITH VITAMIN K
- FATALITY APPROACHES 80%
- IF THEY SURVIVE, RARELY DEVELOPS CHRONIC DISEASE

PREVENTION THROUGH IMMUNOPROPHYLAXIS

- **ACTIVE IMMUNITY**
  - BY STIMULATING OWN IMMUNE RESPONSE
  - PROTECTION AFTER LATENT PERIOD
  - LONG-TERM IMMUNITY IS PROVIDED
- **CAN BE ACCOMPLISHED BY:**
  - ACTUALLY HAVING DISEASE
  - SUCCESSFUL IMMUNIZATION

PREVENTION THROUGH IMMUNOPROPHYLAXIS

- **PASSIVE IMMUNITY**
  - **TRANSFERRING PREFORMED ANTIBODIES FROM AN IMMUNIZED HOST TO A PERSON IN NEED OF IMMUNITY**
  - **PROTECTION IS TRANSITORY, BUT ONSET IS IMMEDIATE**
- **INJECTION OF IMMUNE GLOBULIN (HBIG)**

HEPATITIS B VACCINE

- **PLASMA-DERIVED VACCINE**
  - **HEPTAVAX-B**
  - **THREE SEPARATE 20- µg INTRAMUSCULAR INJECTIONS**
  - **FIRST TWO 1 MONTH APART AND THE THIRD AT 6 MONTHS**
  - **96% YOUNG ADULTS SEROCONVERT**

HEPATITIS B VACCINE

- RECOMBINANT DNA VACCINES
  - RECOMBIVAX HB
  - ENGERIX - B
- PRODUCED BY RECOMBINANT DNA TECHNOLOGY USING YEAST
- SEROCONVERT 99% HEALTHY ADULT 20-29 YEARS OLD

HEPATITIS B VACCINE

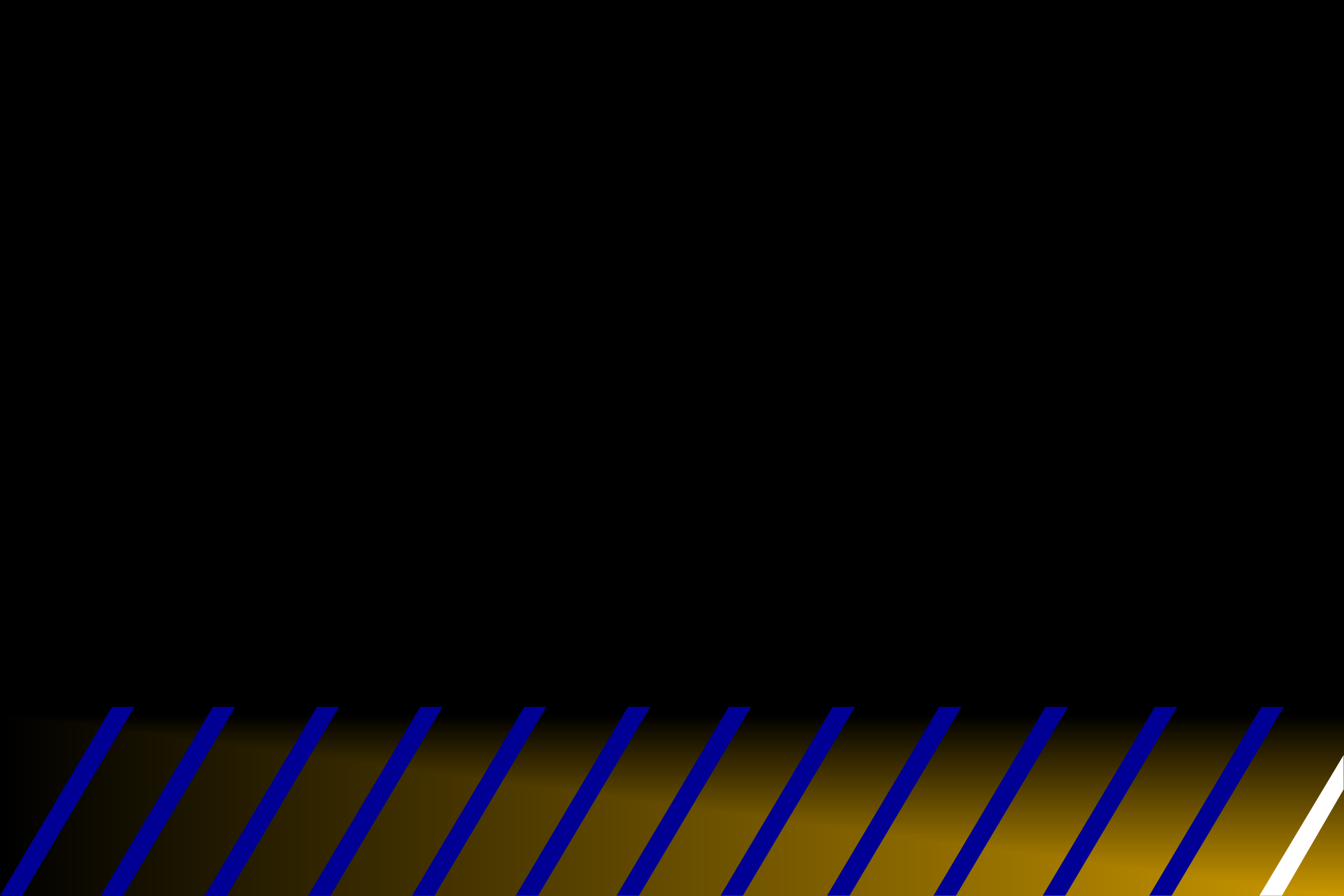
- BOTH PROTECT AGAINST ACTIVE HEPATITIS B, ASYMPTOMATIC HBV, THE CARRIER STATE, AND HDV
- SEROLOGIC TESTING WITHIN 6 MONTHS AFTER COMPLETING SERIES CAN DIFFERENTIATE THOSE THAT RESPOND AND FAIL TO RESPOND TO VACCINE
- 90-95% EFFECTIVENESS

HEPATITIS B VACCINE

- A RECIPIENT WHO IS NEGATIVE FOR ANTI-HBs BETWEEN 1-5 YEARS AFTER VACCINATION CAN BE:
  - VACCINE NON-RESPONDER AND STILL SUSCEPTIBLE TO HBV
  - RESPONDER WITH LESS THAN DETECTABLE ANTI-HBs BUT IS STILL PROTECTED AGAINST CLINICAL DISEASE

POST-TESTING

- NEED POST TEST WITHIN 6 MONTHS OF COMPLETING PRIMARY SERIES
- GREATER THAN 6 MONTHS RESULTS DIFFICULT TO INTERPRET
- REVACCINATION IS SUCCESSFUL FOR NON-RESPONDERS ~ 50%



ANTIBODY PERSISTENCE AND BOOSTER ?

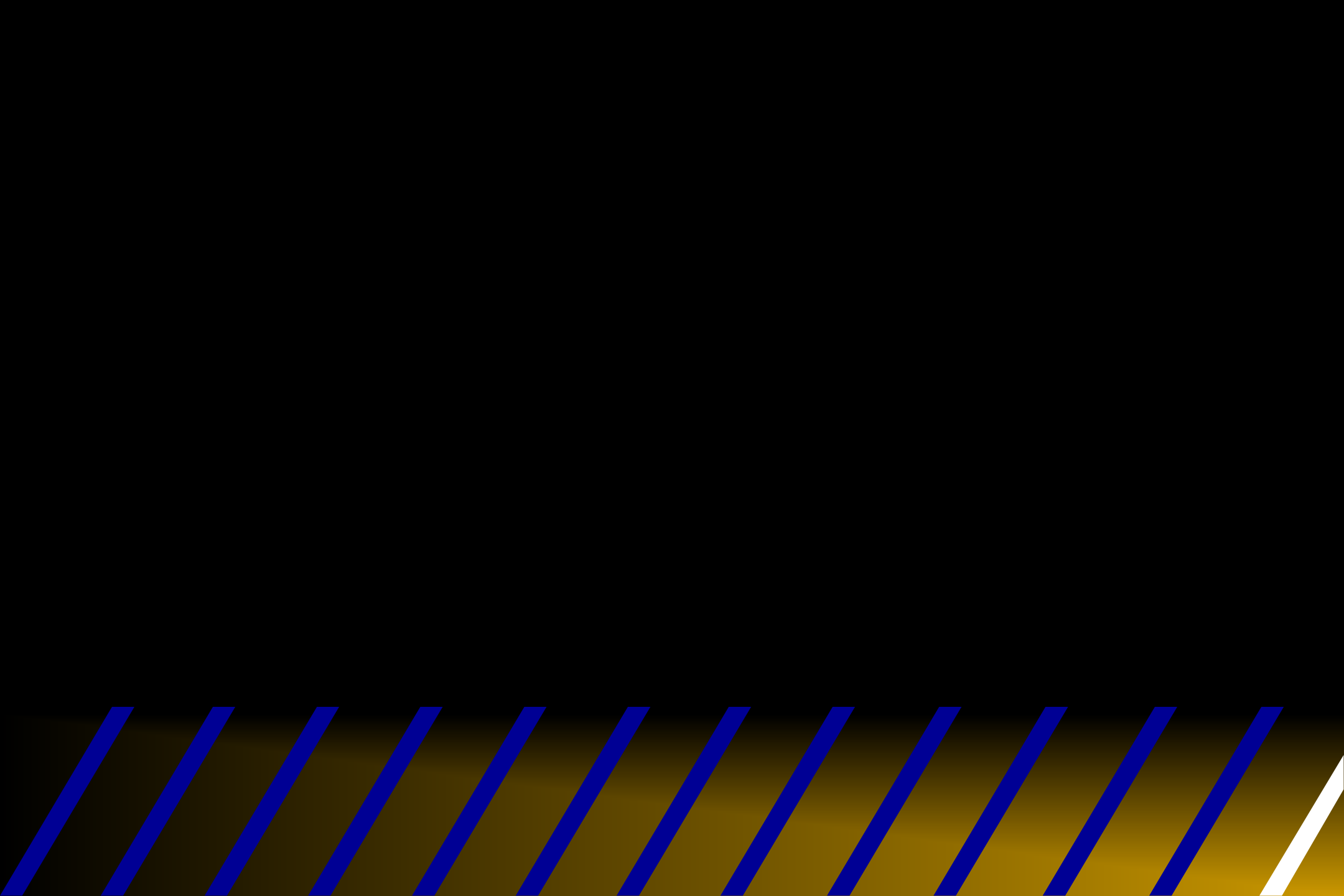
- 70% WHO DEVEOLP ANTI-HBs, MAINTAIN DETECTABLE TITERS FOR 5-7 YEARS (Some say 10 yrs)
- THOSE THAT RESPOND, BUT LOST DETECTABLE ANTI-HBs HAVE DEMONSTRATED A SECONDARY ANAMNESTIC RESPONSE

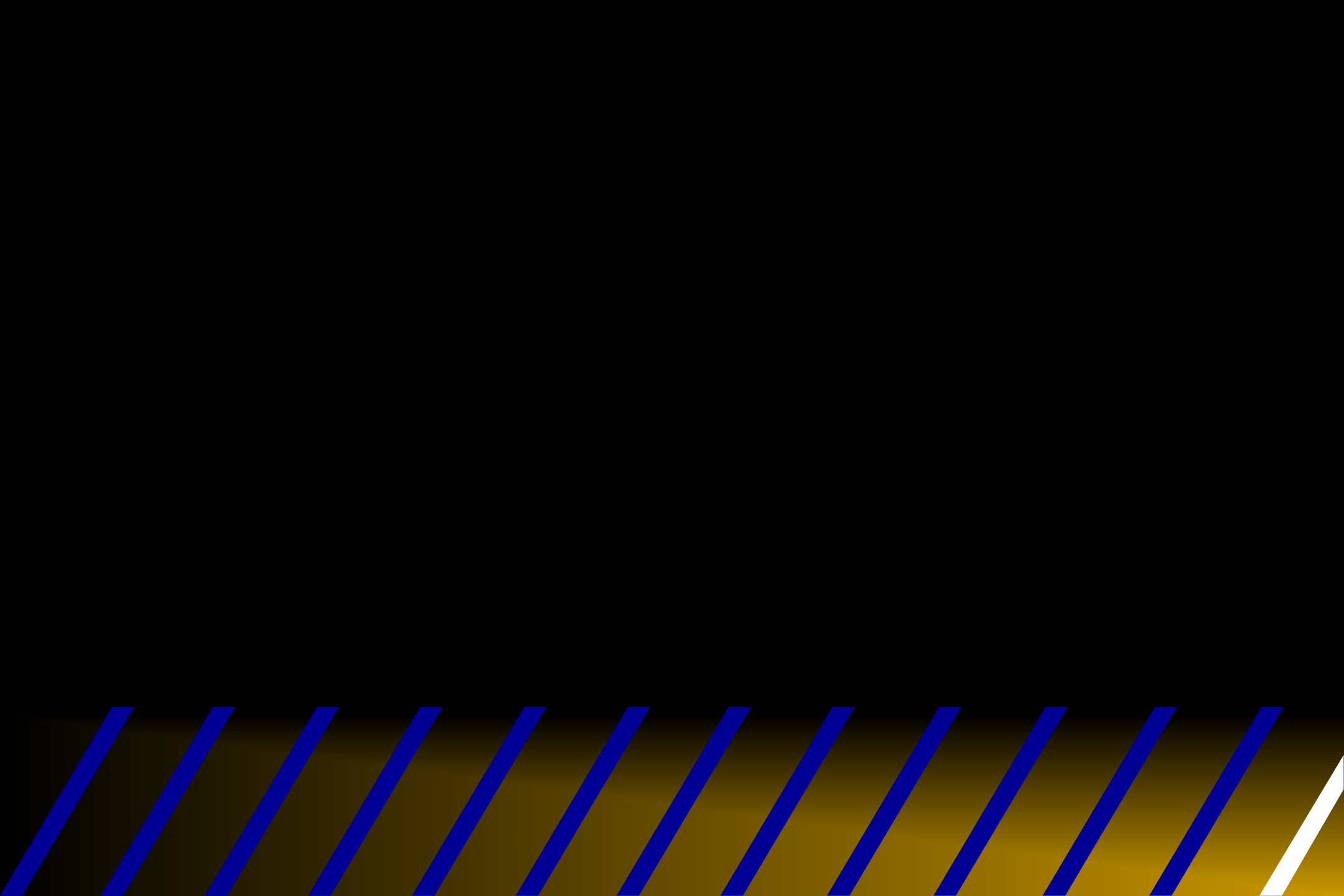
ANTIBODY PERSISTENCE AND BOOSTER ?

- CDC REVIEWING DATA CONCERNING BOOSTER DOSE
- RECOMMEND TITER DRAWN (HbSAb)
- TO DATE, NO ONE WHO HAS RECEIVED A U.S. LICENSED VACCINE, SEROCONVERTED, DEVELOPED ANTI-HBs, WAS IMMUNOCOMPETENT, HAS DEVELOPED CLINICAL HEPATITIS

HEPATITIS A VACCINE

- 2 VACCINES - HAVRIX, VAXTA
- BOTH DERIVED FROM INACTIVATED HAV
- STIMULATE IMMUNE SYSTEM TO PRODUCE ANTIBODIES TO THE VIRUS





HEPATITIS A VACCINE

- GIVEN IN DELTOID MUSCLE
- TWO DOSES - SECOND ONE GIVEN 6 MONTHS TO 1 YEAR AFTER THE FIRST DOSE
- FULL COURSE - CONFERS IMMUNITY IN 100% OF PATIENTS
- NO GUIDELINES FOR BOOSTERS YET

SOURCE: RN December 1997

PREVENTION STRATEGY - HAV

- WASH HANDS BEFORE EATING OR PREPARING FOOD, AND AFTER USING THE BATHROOM, CHANGING A DIAPER, OR CLEANING SURFACES CONTAMINATED WITH FECES
- DON'T EAT UNCOOKED SHELLFISH, SUCH AS RAW OYSTERS AND CLAMS

SOURCE: RN December 1997

PREVENTION STRATEGY - HBV, HCV, HDV

- PRACTICE SAFE SEX
- CLEAN BLOOD SPILLS WITH BLEACH
- DON'T SHARE RAZORS, TOOTHBRUSHES, NAIL CLIPPERS or NEEDLES
- WHEN GETTING A MANICURE, TATTOO, or HAVING A BODY PART PIERCED, MAKE SURE THE INSTRUMENTS ARE STERILE

 SOURCE: RN December 1997

PREVENTION STRATEGY - HEV

- WHEN TRAVELING:
  - DRINK ONLY BOILED, BOTTLED or PROPERLY TREATED WATER (THIS ALSO APPLIES TO ICE CUBES)
- DON'T EAT UNCOOKED SHELLFISH or UNCOOKED FRUITS and VEGTABLES THAT HAVEN'T BEEN PEELED
- DON'T SWIM OR BATHE IN POTENTIALLY CONTAMINATED WATER

SOURCE: RN December 1997

INCUBATION PERIOD

		AVERAGE
HAV -	15 - 45 DAYS	30 DAYS
HBV -	45 - 180 DAYS	60-90 DAYS
HCV -	14 - 180 DAYS	56 DAYS
HDV -	45 - 180 DAYS	
HEV -	15 - 60 DAYS	40 DAYS

 SOURCE: RN December 1997

ONSET

HAV - ABRUPT
HBV - INSIDIOUS
HCV - INSIDIOUS
HDV - ABRUPT
HEV - ABRUPT

 SOURCE: RN December 1997

TRANSMISSION

HAV - FECAL-ORAL ROUTE

HBV - BLOODBORNE, SEXUAL CONTACT, PERINATAL

HCV - BLOODBORNE, PERINATAL, SEXUAL CONTACT LESS LIKELY

HDV - MOSTLY BLOODBORNE - OCCURS AS EITHER A CO-INFECTION WITH HBV OR SUPERINFECTION

HEV - FECAL-ORAL ROUTE

SOURCE: RN December 1997

SIGNS AND SYMPTOMS

HAV - FEVER, MALAISE, ANOREXIA, ANUSEA, ABDOMINAL PAIN and JAUNDICE. OFTEN CHILDREN HAVE NO SYMPTOMS

HBV - DECREASED APPETITE, NAUSEA, VOMITIN, FEVER, WEAKNESS, MALAIZE, MUSCLE ACHES, ABDOMINAL PAIN, JAUNDICE DARK URINE AND CLAY COLORED STOOL, CAN BE SEVERE OR ASYMPTOMATIC

HCV - SIMILAR TO HBV, BUT USUALLY NOT SEVERE

HDV - SAME AS HBV

HEV - SAME AS HBV

SOURCE: RN December 1997

CARRIER STATE

HAV - NONE
HBV - DEVELOPS IN 6 - 10% OF PATIENTS
HCV - 40 - 60 % OF ADULTS BECOME CARRIERS
HDV - USUALLY NONE
HEV - NO KNOWN CARRIER STATE

 SOURCE: RN December 1997

CHRONIC DISEASE

HAV - DOES NOT DEVELOP

HBV - CHILDREN UNDER 5 - 20 - 50%

AGE ABOVE 5 5 - 10%

HCV - 85% OR GREATER

HDV - DEVELOPS MOST OFTEN WHEN HDV IS A SUPERINFECTION

HEV - NO KNOWN CHRONIC INFECTION

 SOURCE: RN December 1997

COMPLICATIONS

HAV - RELAPSE; IN RARE CASES - FULMINANT HEPATITIS

HBV - CHRONIC LIVER DISEASE INCLUDING CIRRHOSIS, PRIMARY HEPATOCELLULAR CARCINOMA AND FULMINANT HEPATITIS

HCV - CHRONIC LIVER DISEASE INCLUDING CIRRHOSIS, PRIMARY HEPATOCELLULAR CARCINOMA

HDV - CHRONIC LIVER DISEASE WITH CIRRHOSIS, LIVER CANCER AND FULMINANT HEPATITIS ALSO POSSIBLE

HEV - DEATH IN ABOUT 20% OF PREGNANT WOMEN

SOURCE: RN December 1997

TREATMENT

HAV and HEV- ACUTE: SYMPTOMATIC

HBV - ACUTE: SYMPTOMATIC

CHRONIC: INTERFERON ALPHA- 2b

HCV - ACUTE: SYMPTOMATIC

CHRONIC: COMBINATION INTERFERON ALPHA 2a and

ALPHA 2b or INTERFERON ALPHA 2a and RIBAVIRON

HDV - ACUTE: SYMPTOMATIC CHRONIC: COMBINATION

INTERFERON ALPHA 2a and ALPHA 2b

SOURCE: RN December 1997

SUMMARY

- VIRAL INFECTIONS MOST IMPORTANT CAUSE OF LIVER DISEASE
- SO FAR SIX HETATITS VIRUSES ARE RESPONSIBLE FOR MOST CASES OF VIRAL HEPATITIS
- SEROLOGICAL and/or MOLECULAR TECHNIQUES ENABLE SPECIFIC IDENTIFICATION OF THESE VIRAL AGENTS
- HBV, HCV, HDV and HGV INFECTION FREQUENTLY PROGRESS TO CHRONIC HEPATITIS, LIVER CIRROSIS

SUMMARY

- HBV, HCV, HDV and HGV INFECTION FREQUENTLY PROGRESS TO CHRONIC HEPATITIS AND OVER TIME TO LIVER CIRROSIS AND HEPATOCELLULAR CARCINOMA
- LONG TERM REMISSION AFTER IFN-α THERAPY IS SEEN ONLY IN A MINORITY OF PATIENTS
- NEED TO DEVELOP:
  - MORE EFFECTIVE ANTIVIRAL THERAPIES
  - VACCINES AGAINST HCV AND POSSIBLY HGV

CONCLUSIONS / RECOMMENDATIONS

- **BEST APPROACH**
  - **GOOD BARRIER TECHNIQUES**
  - **PREVENTION WITH VACCINATION**
  - **UNIVERSAL PRECAUTIONS**

QUESTIONS
?

QUESTIONS???

PLEASE DON'T

SHOOT FIRST AND ASK QUESTIONS LATER !

THINGS TO COME....

- **THERAPY FOR HEPATITIS**
  - **monoclonal antibodies against HbSAg**
- **HBVAg**
  - **specific T-cells**
- **Antiviral Agents**
  - **Interleukin-2, Gamma Infereron, Acyclovir, Gancyclovir, Suramin**